REMARKS

Claims 23, 44 and 45 are currently amended. It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. The Rejection of Claims 23, 25, 26, 28, 33, 34, 36, 38, 39, 43, 44, 45 and 46 under 35 U.S.C. 112 (Written Description)

Claims 23, 25, 26, 28, 33, 34, 36, 38, 39, 43, 44, 45 and 46 stand rejected under 35 U.S.C. 112, first paragraph as allegedly failing to comply with the written description requirement. The Examiner contends that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention. More specifically, the Examiner contends, *inter alia*, that the claims are drawn to a genus of methods using a secretion stress inducible promoter, or using a secretion stress inducible promoter which is in its normal position linked to a gene encoding a polypeptide which has at least 90% or 95% identity to the amino acid sequence of SEQ ID NO:2.

Notwithstanding the amendments above, the rejection is respectfully traversed. The written description must "clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991) (*citing In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989)). In other words, the test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date. *Id.* (*quoting Ralston Purina Co. v. Far-Mar-Co, Inc.*, 772 F.2d 1570, 1575 (Fed. Cir. 1985)); see also *In re Kaslow*, 707 F.2d 1366, 1375 (Fed. Cir. 1983). Quoting *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Company*, No. 2008-1248 (Fed. Cir. Mar. 22, 2010) (*en banc*).

The test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art. Based on that inquiry, the specification must describe an invention understandable to that skilled artisan and show that the inventor actually invented the invention claimed. *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Company*, No. 2008-1248 (Fed. Cir. Mar. 22, 2010) (*en banc*).

Determining whether a patent complies with the written description requirement will necessarily vary depending on the context. *Capon v. Eshhar,* 418 F.3d 1349, 1357-58 (Fed. Cir. 2005). Specifically, the level of detail required to satisfy the written description requirement varies depending on the nature and scope of the claims and on the complexity and predictability

of the relevant technology. *Id.* For generic claims, the Court of Appeals for the Federal Circuit have set forth a number of factors for evaluating the adequacy of the disclosure, including "the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue." *Id.* at 1359. *See Ariad Pharmaceuticals, Inc. v. Eli Lilly and Company*, No. 2008-1248 (Fed. Cir. Mar. 22, 2010) (*en banc*).

The written description requirement does not demand either examples or an actual reduction to practice; a constructive reduction to practice that in a definite way identifies the claimed invention can satisfy the written description requirement. *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1366-67 (Fed. Cir. 2006). *See Ariad Pharmaceuticals, Inc. v. Eli Lilly and Company*, No. 2008-1248 (Fed. Cir. Mar. 22, 2010 (*en banc*).

Applicants respectfully submit that the specification provides adequate written description support for the claimed invention.

Initially, the Examiner has erred by failing to take into account the sequence listings provided herein. Importantly, SEQ ID NO: 1 specifically shows the secretion stress inducible promoter including the nucleic acids 1-999 of SEQ ID NO.:1 or the ykdA promoter region. In addition, SEQ ID NO:1 includes an intact copy of the ykdA gene (nucleic acids 1000-2349 of SEQ ID NO.: 1). Moreover, SEQ ID NO: 1 shows the amino acid sequence for ykda protein also disclosed in SEQ ID NO:2. Clearly, SEQ ID NO:1 provides a secretion stress inducible promoter which is in its normal position linked to a gene encoding the amino acid sequence of SEQ ID NO:2.

Further, page 2, lines 24-29 of the specification states:

> In a third aspect, the invention relates to a method where the inducible promoter is comprised by or comprises the nucleic acids 1-999 of SEQ ID NO.:1.
> In a fourth aspect, the invention relates to a method where the inducible promoter is in its normal position the promoter linked to a gene encoding a polypeptide which has at least 70%, preferably 80%, or 90% or 95% or 98% identity to the amino acid sequence of SEQ ID NO.:2.

Given the maturity of the science, and that the specification provides: SEQ ID NOS: 1 and 2, and the language from the specification as a whole, one of skill in the art would understand that Applicants were in possession of the claimed secretion stress inducible promoters. Reconsideration is urged.

II. The Rejection of Claims 23, 25, 26, 28, 30, 31, 33, 34, 36, 38, 39, 41-46 under 35 U.S.C. 112 (Indefiniteness)

One of ordinary skill in the art would understand the meaning of the term "unknown secreted protein" from the specification. The essential inquiry for determining indefiniteness is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness must be analyzed in light of the claim interpretation that would be given by one possessing the ordinary skill in the pertinent art at the time the invention was made. (M.P.E.P. 2173.02) One of ordinary skill in the art would certainly understand that the phrase "unknown secreted protein" means that the secreted protein is not known.The language of claims 23 and 45 is clear. Reconsideration is urged.

Claim 44 is currently amended and clear. Reconsideration is urged.

III. The Rejection of Claims 23, 25, 26, 28, 39, 43 and 44 under 35 U.S.C. 102(a)

Claims 23, 25, 26, 28, 39, 43 and 44 stand rejected as anticipated by FASEB Journal, 17, No. 4-5, 2003, Abst. No.369.8 (hereinafter referred to as "Griffith I") and FEBS LETT.2003, 553 (1-2), pp.45-50 (hereinafter referred to as "Griffith II"). Independent claim 23 requires, *inter alia*, a method of screening a gene library comprising at least one gene encoding an unknown secreted protein . . . selecting a host cell which expresses the reporter protein or regulator protein and comprises the gene encoding the unknown secreted protein. Conversely, Griffith I and Griffith II disclose host cells with different copy numbers of an integrated Tep2 vector which does not include at least one gene encoding an unknown secreted protein. Accordingly, Griffith I and Griffith II do not anticipate the claimed invention. Reconsideration is urged.

Claim 45 is currently amended and is not anticipated by Griffith I or Griffith II. Reconsideration is urged in light of the amendments herein and comments above.

IV. The Rejection of Claims 23, 25, 26, 28, 39, 43 and 44 under 35 U.S.C. 102(b)

Claims 23, 25, 26, 28, 39, 43 and 44 stand rejected as anticipated by Jones et al. (Embo J. 16, 6394-6406, 1997) (hereinafter referred to simply as "Jones").

Independent claims 23 and 45 refer to a method of screening a gene library comprising at least one gene encoding an unknown secreted protein . . . each method requiring selecting a host cell which expresses the reporter protein or regulator protein and comprises the gene encoding the unknown secreted protein. Initially, Applicants respectfully submit that separate and independent over expression of a gene, encoding PapE or PapG does not relate to the screening of a gene library which would generally show simultaneous over expression. For this reason alone,

Applicants submit that the reference is deficient. Further, even if for the sake of argument two genes make up a library (which applicant's do not concede) a library including PapE or PapG does not include a gene encoding the unknown secreted protein as required by the claimed invention. Accordingly, no claim is anticipated. Reconsideration is urged.

V. The Rejection of Claims 30, 31, 33, 34, 36, 38, 41, 42, 45 and 46 under 35 U.S.C. 103(a)

Claims 30, 31, 33, 34, 36, 38, 41, 42, 45 and 46 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Lesley et al., Protein Eng. 15, pp. 153-160 (2002) ("Lesley") or Waldo, Curr. Opin. Chem. Biol., 7, pp. 33-38 (2003) ("Waldo") in view of Noone, J. Bacteriol., 183(2), pp. 654-663 (2001) ("Noone"). Applicants traverse this rejection.

"Section 103 forbids issuance of a patent when 'the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.'" *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 298, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations including (1) the scope and content of the prior art, (2) any differences between the claimed subject matter and the prior art, (3) the level of skill in the art, and (4) where in evidence, so-called secondary considerations. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966). The Supreme Court stated that "[o]ften, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue." *KSR*, 550 U.S. at 418. The Court also noted that "[t]o facilitate review, this analysis should be made explicit." *Id.* at 418. (Citing *In re Kahn*, 441 F.3d 977, 988 (Fed Cir. 2006) ("[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness")). However, "the analysis need not seek out precise teachings directed to a specific subject matter of the challenged claim, for a court can take into account of the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.*

Further, general statements lack the specificity required to support a legal conclusion of obviousness and are thus insufficient to establish *prima facie* obviousness. See KSR (holding that a "patent composed of several elements is not proved obvious merely be demonstrating that each of its elements was, independently, known in the art . . . it can be important to identify

a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed invention does."

In rejecting claims under 35 U.S.C. § 103(a), the examiner bears the initial burden of establishing a *prima facie* case of obviousness. *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir 1992); *see also In re Piasecki*, 745 F.2d 1468, 1472 (Fed. Cir. 1984). Only if this initial burden is met does the burden of coming forward with evidence or argument shift to the appellant. *See Oetiker*, 977 F.2d at 1445; see *also Piasecki*, 745 F.2d at 1472. Obviousness is then determined on the basis of the evidence as a whole and the relative persuasiveness of the arguments. *Id*.

The Examiner has failed to make a *prima facie* case of obviousness, and the rejection is in error.

The present disclosure solves problems associated with screening methods for unknown secreted proteins. Applicants have made a novel contribution to the art by disclosing an industrially relevant screening method.

On page 9 of the Official Action, the Examiner has concluded, the "instant application differs from Lesley et al. or Waldo in that secreted proteins are concerned. However Noone et al disclose the secretion stress promoter disclosed in the instant claims. It would have been obvious to one of ordinary skill in the art to have substituted the promoter disclosed by Noone et al. in the methods disclosed by Lesley et al. or Waldo, since all of the references disclose promoters operatively linked to reporter genes, that response to environmental conditions or stress induced by expression of particular types of proteins. One would have been motivated to do so by the desire to screen for secreted proteins, which is known to be useful for ease of production and purification of the protein produced. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention." Applicants note that the Examiner's rejection is deficient in that it fails to sufficiently identify a sufficient reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed invention does. There is no indication from the art that these references would be combined to obtain a working configuration in accordance with the present disclosure especially where the art is unpredictable. Reconsideration is urged.

Further, the Examiner has not provided a reason of why the disclosures of the references should be combined. The cited references are devoid of any suggestion to combine the teachings and suggestions of Lesley, Waldo or Noone as advanced by the Examiner, except from using Applicants' disclosure as a template through hindsight reconstruction of Applicants

claim. Thus, the Examiner has erroneously retraced the path of the inventor with hindsight -- discounting the number of complexities of the alternatives in order to conclude that the specifically claimed methods were obvious. This reasoning is always inappropriate for an obviousness test based on the language of Title 35 that requires the analysis to examine "the subject matter as a whole" to ascertain if it "would have been obvious at the time the invention was made." 35 U.S.C. § 103(a).

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 103. Applicants respectfully request reconsideration and withdrawal of the rejection.

VI. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

All required fees were charged to Novozymes North America, Inc.'s Deposit Account No. 50-1701 at the time of electronic filing. The USPTO is authorized to charge this Deposit Account should any additional fees be due.

Respectfully submitted,

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/Michael W. Krenicky, Reg. # 45411/

Michael W. Krenicky, Reg. No. 45,411
Novozymes North America, Inc.
500 Fifth Avenue, Suite 1600
New York, NY 10110
(212) 840-0097